

REMARKS

Status of the Claims

Claims 1-15, 27-29 and 31-37 were pending in the application. Claims 5, 7, 10, 12, and 15 were amended. Claims 1-4, 6, 8, 9, 11, 13, 14, 27-29, 31-37 have been canceled without prejudice. Claims 38-64 have been added. Upon entry of this amendment Applicants claims 5, 7, 10, 12, 15, and 38-64 will be pending.

Summary of the Amendment

Claims 5, 7, 10, 12, and 15 have been amended to remove the term "pure." Claims 38-64 have been added. Support for the new claims can be found throughout the specification and the as-filed claims. No new matter has been added.

Claim Objections

Claim Rejections Under 35 U.S.C. §112, Second Paragraph

Claim 14, stand rejected under 35 U.S.C. §112, second paragraph, for allegedly failing to comply with and particularly point out and distinctly claim the subject matter of the current invention. The Office alleges that claim 14 is indefinite for the recitation of the terms "Pm promoter" and "xylS gene." The Office alleges that one of skill in the art would not understand what is meant by these terms. Applicants respectfully disagree.

Applicants note that claim 14 has been canceled, but other claims, such as new claims 54-56 retain these terms. Applicants also note The claims are definite because one of skill in the art would understand what is meant by these terms. Applicants have enclosed herewith two references that make clear that one of skill in the art would understand what the terms "Pm promoter" and "xylS gene" mean. For example, in Ramos *et al.* (*Annual Rev. Rev. Microbiol.* (1997) 51:341-372, hereinafter "Ramos reference") the xylS gene is described. The Ramos reference describes the *xyl* genes of TOL plasmids of a pseudomonas species. It is clear from the Ramos reference that the TOL plasmids are well known plasmids that encodes enzymes for

the degradation of toluates and xylenes. The enzymes of these catabolic pathways are encoded by two operons which comprise the *xyI* genes. *XyIS* is a regulatory gene which acts to regulate the expression of the inducible promoter Pm (page 345, paragraph 3). As is clear from the Ramos reference the Pm promoter and its regulatory gene *xyIS* are well known and widely described in the art and moreover, expression system based on the Pm and *xyIS* system are also known.

Additionally, in Larsen *et al.* (*Metabolic Engineering* (2000) 2: 92-103, hereinafter "Larsen reference") describes a Pm promoter expression mutants and their use in broad-host-range RK2 plasmid vectors. The Larsen reference describes expression vectors based on the Pm/*xyIS* promoter system. The Larsen reference simply refers to the elements of the system using the terms Pm and *xyIS* and these terms are readily understood by any person skilled in the art.

The terms Pm and *xyIS* are also used in patents and patent applications and that the terms are understood by one of skill in the art. For example, in U.S. Patent No. 6,258,565 the terms "Pm promoter" and "*xyIS* gene" are extensively used in both the specification and the claims. Additionally, PCT Publications WO/2000/068375 and WO 2008/01544 refers to mutants of the Pm promoter and also uses the terms and also refers to expression systems based on, *inter alia*, Pm and *xyIS*.

Accordingly, one of skill in the art would understand what is meant by the term "Pm promoter" and "*xyIS* gene" because they are universally used and understood to refer to a specific promoter and a specific gene as understood by the skilled artisan.

Applicants respectfully request the rejection of claims reciting the terms "Pm promoter" and "*xyIS* gene" under 35 U.S.C. §112, second paragraph be withdrawn.

Claims 2-4 were rejected as allegedly being unclear for the recitation of the phrase "A biologically pure." Applicants respectfully disagree that the term is indefinite, but in view of the amendments to the claims where this phrase is no longer used and claims 2-4 have been canceled

the rejection is moot. Accordingly, Applicants respectfully request that the rejection of claims 2-4 be withdrawn.

Claim Rejections Under 35 U.S.C. §112, First Paragraph

Written Description

Claims 1-4, 6, 8, 9, 11, 13, 14, 27-29, 31, and 33-37 stand rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the art that the inventors, at the time of the application was filed, has possession of the claimed invention. The Office alleges that because the specification only discloses a few mutant strains of *P. fluorescens* and that because these mutants do not represent all mutant strains within the scope of the pending claims the skilled artisan cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed. The Office alleges that possession cannot be shown because the specification does not teach the structures of all C-5 epimerase, algG-gene and other alginate biosynthetic pathway genes nor teaches how all *P. fluorescens* will be modified. The Office alleges that the strains disclosed in the present specification are “not representative of all the structure and/or function of all strain[s] encompassed by the instant claims.” Therefore, the Office alleges that “given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.” Applicants respectfully disagree.

The pending claims satisfy the written description requirement because one of skill in the art would understand that Applicants were in possession of a mutant strain of *P. fluorescens* being strain Pf201 or a variant thereof or a mutant strain of *P. fluorescens* which has the characteristics of strain Pf201 in relation to alginate production, wherein said variant or mutant strain produces at least 10 g alginate per liter medium and is stable over at least 60 generations.

As an initial matter Applicants respectfully note that the Office is misinterpreting the specification and the claims. The Office refers repeatedly to mutations in one or more of the alginate biosynthetic pathway genes such as, for example, the epimerase and *algG* genes. It is important to note that the specific genes which are mentioned in the description and the claims, namely *algG* encoding epimerase, *algL* encoding alginate lyase and *algL*, *algJ* and *algF* encoding genes relating to acetylation of the alginates, are not genes the mutation of which would result in a modification in the amount of alginate produced by the *P. fluorescens*, or indeed genes the mutation of which would convert a *P. fluorescens* non-alginate producer to being a producer of alginate. These latter genes, as has been previously discussed, encode enzymes which affect the nature or quality of the alginate in terms of its G content, its molecular weight, and its acetylation, but do not directly relate to production of the alginate *per se* (in terms of whether or not, or how much, alginate is produced).

The Office appears to require that the specification and the claims refer to specific mutations in specific genes for all species to comply with the written description requirement. The Office's standard for compliance with the written description requirement is incorrect. In the recent decision by the Court of Appeals for the Federal Circuit in *Bilstad v. Wakalopoulos* 386 F.3d 1116, 1125 (Fed. Cir. 2004), the court found that the Board failed to apply the proper standard for determining the sufficiency of the written description requirement. The court stated that that disclosure of a species may be sufficient written description support for a later claimed genus including that species if the difference between members of the group is such that the person skilled in the art would readily discern that other members of the genus would perform similarly to the disclosed members. In the instant application, the person skilled in the art would readily discern that other members of the genus would perform similarly to the disclosed members.

For example, new claim 38 refers specifically to strain Pf201. New claim 51 refers to a mutant strain of *P. Fluorescens* which comprises a mutant *algG* gene, wherein the *algG* gene is inactivated or encodes an enzyme having reduced epimerase activity. Claim 52 refers to A mutant strain of *P. fluorescens* which produces alginate, wherein in said mutant strain the

alginate biosynthetic operon has been placed under the control of an inducible promoter which replaces the native promoter of said operon. These independent claims all refer specifically to a gene or operon and a function associated with that strain being claimed. These claims do not refer generally to only a function or end result that is desired. Instead the claims when read in view of the specification and the examples show possession of the claimed invention at the time the application was filed.

The specification provides adequate written description. Applicants respectfully note that the issue of modification of these genes is, therefore, not directly relevant to the issue of new claim 38 which defines a mutant strain of *P. fluorescens* which is able to produce alginate at a particular level and is stable over at least 30 generations with respect to this alginate production characteristic. In this respect, as noted at page 1, lines 25 to 30, the production of stable over-producers of alginate in non-pathogenic species of *Pseudomonas* such as *P. fluorescens*, is the object of the present invention. In order to obtain such alginate over-producers, the specification describes two methods which may be used, which indicates that Applicants had possession of the present invention.

The first method is to randomly mutagenize wild-type *P. fluorescens* organisms and then to screen the mutants to identify alginate over-producers. This is described in detail in the specification – see, for example, Example 1. The second method as described at page 5, lines 13 to 22 is to place the alginate biosynthetic operon under the control of an inducible promoter which replaces the native, naturally occurring, promoter of the operon. In this way, the expression of the alginate biosynthetic operon may be induced or “switched-on”, in order to turn the modified organism into an alginate producer. This latter method is reflected in new claim 52. With specific regard to claim 52, the specification describes in detail how such a method may be carried out and accordingly provided a full written description of such a method. The specification also contains procedures and examples of strains within the specific claims. (See examples 1, 2, 6, 7, and 8). The Office’s apparent requirement that the invention be limited to only the strains or mutants described is incorrect. As stated above, in view of the specification,

which must be read as a whole, one of skill in the art would be able to readily discern that the members of the genus would perform the same as the species disclosed.

Therefore, one of skill in the art, reading these methods and the other examples contained in the specification demonstrating the species with the claimed functionality, would readily discern that Applicants were in possession of the genus when the application was filed.

Therefore, in view of the amendments to the claims read in view of the specification one of skill in the art would understand that Applicants were in possession of the claimed invention at the time the application was filed. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph as allegedly not complying with the written description requirement be withdrawn.

***Claim Rejections Under 35 U.S.C. §112, First Paragraph
Enablement***

Claims 1-4, 6, 8-9, 11, 13-14, 27-29, 31, and 33-37 are rejected under 35 U.S.C. § 112, first paragraph because the specification, while being enabling for the few mutant strains of *P. fluorescens* (e.g. as those recited in claim 5) the specification allegedly does not reasonably provide enablement for any mutant strain of *P. fluorescens*, produced by mutating one or more alginate biosynthetic pathway genes by any means. The Office alleges that the specification fails to describe how any *P. fluorescens* strain can be mutated by any means to produce alginate in the recited levels. Applicants respectfully disagree.

Applicants note that the claims rejected in the present office action have been cancelled and new claims have been added. In view of the amendments Applicants respectfully request that the enablement rejection be withdrawn. The reasoning used by the Office in rejecting claims 1-4, 6, 8-9, 11, 13-14, 27-29, 31, and 33-37 as allegedly not being enabled does not apply to the present claims. For example, new claim 38 refers specifically to strain Pf201 or a strain that has the characteristics of strain Pf201, wherein the strain produces at least 10 g alginate per liter medium and is stable over at least 60 generations. New claim 51 refers to a strain comprising a mutant *algG* gene and produces alginate having a defined guluronate residue (G)-content between 0 and 30%, wherein said *algG* gene is inactivated or encodes an enzyme having reduced

epimerase activity. New claim 52 refers to a mutant strain of *P. fluorescens* which produces alginate, wherein in said mutant strain the alginate biosynthetic operon has been placed under the control of an inducible promoter which replaces the native promoter of said operon. One of skill in the art would be able to make such strains without undue experimentation.

As the Office acknowledges recombinant and mutagenesis techniques are known and routine. The Office alleges that “it is not routine in the art” to screen for mutants with certain characteristics as those claimed. (Office action, page 9). The Office, however, in making this conclusory statement refers to no reference or other document to support such a conclusion. The Office also alleges that one of skill in the art “would expect any tolerance to modification for a given protein to diminish with each and further and additional modification.” (Office Action, page 9). However, as with the Office’s previous statement, there is not support for such a conclusion. The Office alleges that “it is not routine in the art to control a gene by any means to obtain desired outcome” and “that controlling one gene without affecting other genes that involve alginate synthesis is difficult.” (Office Action, pages 9-10). The Office, however, has appeared to completely disregard Applicant’s specification as teaching one of skill in the art how to make the strains as described in the pending claims.

In contrast to making statements that are backed up with any evidence, the Office makes generalized statements with no support. As the M.P.E.P states, “in order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention (M.P.E.P § 2164.04 citing *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). It is not enough for the Office to make conclusory statements. The Office must explain why it “doubts the truth or accuracy of any statement in a supporting disclosure and ***to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.***” *In re Marzocchi*, 439 F.2d 220, 224 (C.C.P.A. 1971). The Office has failed to back up its assertions with any evidence let alone “acceptable evidence” that could cast doubt on the enablement of the pending claims. If the Office maintains the rejection based solely upon the Office’s knowledge, Applicants respectfully request that the Office submit an affidavit attesting to such facts. Therefore, the Office has failed

to articulate a sound or adequate reason as to why supported with acceptable evidence to show that the claims are not enabled.

Even if the Office had cited a single reference to cast doubt on the enablement of the present invention, which it has not, contrary to the Office's position the present specification describes several methods of obtaining such mutants and one of skill in the art would be able to use the examples and details in the present specification to make and use the present invention. As discussed above, the issue of modification of the genes identified by the Office is not directly relevant to the issue of new claim 38 which defines a mutant strain of *P. fluorescens* which is able to produce alginate at a particular level and is stable over at least 60 generations with respect to this alginate production characteristic. In this respect, as noted at page 1, lines 25 to 30, the production of stable over-producers of alginate in non-pathogenic species of *Pseudomonas* such *P. fluorescens*, is the object of the present invention. In order to obtain such alginate over-producers, the specification describes two methods which may be used. The first method is to randomly mutagenize wild-type *P. fluorescens* organisms and then to screen the mutants to identify alginate over-producers. This is described in detail in the specification - see for example, Example 1. The second method as described at page 5, lines 13 to 22 is to place the alginate biosynthetic operon under the control of an inducible promoter which replaces the native, naturally occurring, promoter of the operon. In this way, the expression of the alginate biosynthetic operon may be induced or "switched-on", in order to turn the modified organism into an alginate producer. This latter method is reflected in new claim 52. With specific regard to claim 52, the specification describes in detail how such a method may be carried out and accordingly provided a full written description of such a method.

Furthermore, Example 8 makes clear, alginate operons in *Pseudomonas* species had been identified and described in the prior art. As mentioned in the introduction to Example 8, all sequenced alginate-producing species of *Pseudomonas* have the same conserved open reading frame upstream of the alginate promoter. Thus, it is a matter of routine for the skilled artisan to be able to identify the alginate operon within a sequence of the genome of a *P. fluorescens* strain. As Example 8 also indicates, such genomic sequences are publicly available. Example 2 of the

present specification also describes the cloning and sequencing of the alginate biosynthetic operon of a wild-type *P. fluorescens* strain. The sequence has been deposited and is publicly available. Thus, as a matter of routine, the skilled person would be able to identify the alginate biosynthetic operon within a genomic sequence of a *P. fluorescens* strain.

As described in Example 8, the skilled person would further readily be able to identify promoter sequences which lie upstream of *algD*, the first gene in the alginate operon and to replace such sequences with an inducible promoter such as the Pm promoter. As is clear from the above, the Pm promoter is well known and widely described in the literature and hence Pm promoter sequences are readily available to the skilled person. Furthermore, a wide variety of inducible promoters are known and described in the art and would be available to the skilled person. Example 8 also describes how a Pm promoter may be substituted for the native promoter of the alginate operon so as to obtain a modified or mutant strain of *P. fluorescens* in which the alginate biosynthetic operon is under the control of an inducible promoter and in which the production of alginate may be induced.

Example 8 also describes the preparation of a modified strain based on mutant strain PF201. It is clear, however, that such techniques may be used by one of skill in the art with any strain of *P. fluorescens*, including wild-type strains and indeed, the Applicants have carried out experiments using wild-type strains, including wild-type strain NCIMB 10525 (from which mutant strain PF201 was derived) in which the alginate biosynthetic genes are regulated from the Pm promoter.

Example 8 concerns specifically the Pm promoter, and Example 9 describes the identification of mutant Pm promoters. Indeed, mutant Pm promoters have been described in previously. (See, for example, WO 00/68375, WO 2008/015447 and the Larsen *et al* references, attached hereto)

To satisfy the enablement requirement it is not necessary to identify specifically or exactly which particular mutations are made. It is not necessary to know any or all of the genes which might be mutated in order to affect alginate production. It is not critical to know the nature of the mutation. All that is required to practice the invention is to randomly mutate a wild-type

strain of *P. fluorescens* and then to screen the mutants thereby obtained in order to identify mutants which are capable of producing alginate. These are routine methods and the specification provides a detailed description of procedures for carrying out these steps. Thus, the specification describes a procedure for mutagenizing *P. fluorescens* and indeed such mutagenesis procedures are routine in the art.

Also described in Example 1 is the identification of alginate-producing mutants. In other words, a screening procedure is described for identifying the mutants. Thus, cells of wild-type *P. fluorescens* are simply exposed to a known mutagenic agent (specifically nitrosoguanidine in Example 1), the mutagenized cells are then grown overnight and, very simply, the appearance of mucoid mutants may be observed - a mucoid colony will indicate the production of alginate. Thus, a screen for alginate producers is very simple and is described. Furthermore, alginate production may be determined and confirmed by growth of the organisms using the procedures described in the experimental description, for example in relation to growth of *P. fluorescens* in culture and production of alginate. The specification provides details for alginate production in shake flasks and fermentors and describes techniques of the direct measurement of the alginate content in fermentation samples. There is, therefore, a detailed written description of procedures for obtaining the mutants (standard mutagenesis procedures) and for screening the mutants to identify alginate producers. This is all that is required in order to obtain an alginate producing mutant strain of *P. fluorescens* according to claim 38. Thus, it is not appropriate or correct of the Office to require the applicant to describe each and every particular mutation to show that the present invention is enabled.

Here, the present specification describes a ready screen for a mutant having the requisite properties. Furthermore, once a mutant has been obtained, it may be sequenced in order to identify the underlying mutation (by comparison to the un-mutated non-alginate producing wild-type strain). Once such a mutation has been identified, a corresponding mutation may then subsequently be introduced into a further wild-type strain. As noted above, the Office's references to alteration of five genes mentioned not representing all the variations encompassed by the claims are misplaced - not only are the five specific genes mentioned not directly relevant

to the issue of the amount of alginate produced (they control G content, molecular weight and acetylation), for the reasons described above it is not necessary to know what the exact mutation is.

The Office admits that enablement is not precluded by the necessity for routine screening (Office Action, page 13) but the Office alleges that if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Applicants have provided such guidance. The Office appears to allege that one of ordinary skill in the art would not be able to mutagenize strains of *P. fluorescens* using the methods described in the present specification or otherwise known and then characterize them using the methods described in the present specification. As discussed above, the Office has not provided a single reference that says such methods would not be routine. The Office appears to correlate undue experimentation with amount of experimenting done. This standard, however, is improper.

In *In re Wands*, where the standard of enablement was stated extensive screening was done based upon characteristics of the products being claimed and yet such screening was held to be routine and not present an undue burden. Here, the situation is the same. The present specification describes how to make strains of *P. fluorescens* and how to characterize them. All that is required to practice the claimed invention is routine experimentation based upon the present specification.

The issue of enablement relates to the ability of the skilled person to be able to reproduce the invention and to obtain a mutant having the specified characteristics. The specification describes methods by which such mutants may be generated and methods by which such mutants may be identified in a screen (see above). This is all that is required for the skilled person to be able to practice the invention. It is not necessary to screen for particular substitutions or modifications to the genetic sequence, but to screen for the desired effect, namely alginate production. The present application describes the screens by which this may readily be done. It is not necessary in order to practice the invention to identify, or to screen for the exact nature of the modification which results in the observed effect.

Unpredictability as to the specific mutation underlying the effect is not relevant to the issue of enablement - as regards predictability of obtaining the effect, the specification shows that mutants may be obtained and identified. Thus, it is predictable that a mutant producing alginate may be obtained. Furthermore, as described above, once such a mutant has been obtained, the mutation within it may be identified and consequently a corresponding mutation may be introduced into another *P. fluorescens* organism. Thus, the provision of Pf201 and the other mutants described, is itself enabling to obtain other mutants producing alginate.

The Office is incorrect to say that there is a necessity for producing and testing all of the virtually infinite possibilities to find out which amino acid residue to modify because, as explained above, there is not such necessity in order to be able to practice the invention. It is not necessary to know what the mutation is, but simply to be able to identify a mutant having the required effect i.e. a mutant capable of producing alginate. The present specification provides a description of a screen for such mutants. Thus, there is not undue experimentation necessary. The present specification provides specific details of an assay which is readily possible to perform to identify alginate producers and furthermore the present application demonstrates that carrying out such a mutagenesis and screening procedure results in the identification of mutant strains having the specified effects.

Furthermore, insofar as mutations to genes of the alginate biosynthetic pathway which modify the nature or quality of alginate are concerned, the specification described in detail various mutants which may be obtained. This is relevant to new claim 51 relating to *algG* mutants and also the dependent claims 43 to 49 and 57 to 63. With particular reference to *algG*, a detailed description of the preparation of *algG* negative mutants is described in Example 3. Table 3 in this example shows that different point mutations may be made in order to achieve inactivation of the *algG* gene. Thus, the precise nature of mutation to inactivate the gene is not critical. Thus, the production of a mutant which produces pure mannuronate is not dependent only on particular mutations and a range of different mutations are possible.

Additionally, Examples 6 and 7 describe the production of mutant strains having reduced, rather than inactivated, epimerase activity. Again, the nature of the precise mutation is not

important - mutations may simply be introduced into *algG* gene using known and well recognized procedures and the effect of such mutations may simply be screened for, again using procedures described in detail in the specification. Example 6 describes a procedure for preparing variant strains with reduced epimerase activity by random mutagenesis to generate to library of mutants. For reasons described above, the exact nature of the mutation is not critical and all that is necessary is to be able to make such mutants and to be able to identify them by screening. Both of these requirements are enabled by the disclosure of the specification as filed. Furthermore, as described at the foot of Example 6, in order to produce further variant mutant strains producing a desired alginate product the mutant genes may be recovered from the mutants identified by screening using known techniques and the mutant genes may then subsequently be transferred into other *Pseudomonas fluorescens* strains.

Example 7 described an alternative procedure for obtaining variant mutant strains with reduced epimerase activity. Thus, according to the procedures described in this example, reduced-epimerase activity mutants obtained by random mutagenesis as described in Example 6 may be subjected to sequencing in order to identify the mutated amino acids. Corresponding mutations or similar mutations at these amino acid positions may then be made by site specific mutagenesis.

Example 4 describes how the genes *algF*, *algI* and *algJ* which are relevant to acetylation of the alginate may be inactivated or modified to reduce enzyme activity and thereby result in the mutant strains which have altered alginate characteristics in terms of acetylation. The procedures described in the Example are enabling for the modification of the *algF*, *algI* and/or *algJ* genes in other strains of *P. fluorescens*. Similarly with the *algL* gene which affects molecular weight of the alginates produced, Example 5 describes procedures for modifying this gene and is therefore enabling for the production of mutant strains which produce alginate of desired molecular weight.

Accordingly, the present specification provides numerous working examples of how to obtain strains and nothing more than routine experimentation is required to practice the claimed

invention. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph with respect to the enablement rejection be withdrawn.

Claim Rejections Under 35 U.S.C. § 102

Claims 1-4, 6 and 33-36 have been rejected under 35 U.S.C. §102(c) as being anticipated by Huisman *et al* (U.S. Patent Application Publication No. 2004/0014197). Applicants respectfully disagree.

The claims are not anticipated because the Huisman reference fails to disclose each and every element as arranged in the pending claims. For a reference to anticipate a claim it must not only disclose each and every element of the claims but the reference must disclose the elements as arranged. Recently, the Federal Circuit has emphasized that a reference that discloses elements that are connected to one another cannot anticipate an invention. In *NET MONEYIN, INC., v. Verisign* (CAFC 2008, Docket No. 2007-1565, decided October 20, 2008) the district court held that a claim was anticipated even though the prior art reference did not disclose the elements as arranged instead the district court combined two examples to produce the claimed invention. The Federal Circuit reversed holding that such a combination does not anticipate a claim. The Federal Circuit held

that unless a reference discloses within the four corners of the document not only all of the limitations claimed ***but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. § 102.***

(*NET MONEYIN* at *17, emphasis added). Here, the Office has done what is improper and accordingly the Huisman reference does not anticipate the pending claims.

The Huisman reference fails to anticipate the pending claims because the reference fails to explicitly or inherently disclose mutant strains of *P. fluorescens* as defined in the present claims. The Office appears to be combining various disparate disclosures in the claims of the Huisman reference. Correctly read, there is no disclosure of an alginate-producing strain of *P. fluorescens*.

In this respect, the description of Huisman refers generally to microbial fermentation for the production of polymers such as a polyhydroxyalkanylates (PHA) and polysaccharides. The invention concerned in Huisman is to express a nuclease in the producing bacterial strain in order to degrade nucleic acids so as to enhance recovery of the desired product (e.g. PHA or polysaccharide). The introductory part of the specification of Huisman refers generally to microbial strains for use in fermentation processes and generally to the production of microbial polysaccharides by fermentation of a number of different microorganisms. At no point is it mentioned explicitly or implicitly that *P. fluorescens* or indeed any *Pseudomonas* strain may be used to produce alginates. Thus, in paragraph 0010, alginates are simply listed as an exemplary polysaccharide. It is not suggested that *P. fluorescens* may be used to produce alginates. Paragraph 0024 discusses that the *Pseudomonas* strains e.g. *P. putida* may be used to produce PHAs, however, Applicants respectfully note that an alginate is *not* a PHA. Paragraph 0025 refers to *Pseudomonas* in connection with PHA production only. Paragraph 0032 refers to the production of polysaccharides generally. It is mentioned here that *Pseudomonas elodea* strains may be used to produce gellan gum. It is also mentioned that alginates may be produced by brown algae and by fermentation of *Azotobacter* strains. There is no mention here of the use of *Pseudomonas* of any species to produce alginates. Similarly paragraph 0034 refers to gellan gum production by *Pseudomonas elodea*. There is no mention here of alginate production by any strain or species of *Pseudomonas*.

Example 2 of the Huisman reference describes the construction of a transgenic *P. putida* strain expressing a nuclease. There is no discussion or suggestion or disclosure that such a transgenic *P. putida* strain may be used to produce alginate. Example 4 relates to PHA accumulation by a transgenic *P. putida* strain expressing a nuclease gene. Example 5 relates to the introduction of genes encoding PHA biosynthetic enzymes into various engineered strains which include certain *Pseudomonas* strains, but not specifically *P. fluorescens* (para 0053). There is no disclosure in this Example of a strain of *P. fluorescens* which produces alginate. As noted above, alginate is *not* a PHA. Thus, it is clear from a detailed consideration of the

description that there is no disclosure whatsoever of a *P. fluorescens* strain which produces alginate.

Insofar as the disclosure of the claims is concerned, the Office's interpretation of what might be disclosed by combining various claims is quite simply inappropriate and a disclosure of a *Pseudomonas fluorescens* strain producing alginate at the specified levels cannot be derived. Claim 1 of the Huisman reference refers generally to production of the various products including polysaccharides. Claim 3 which is indirectly dependent on claim 1 refers to the production of polyhydroxyalkanoate to levels of at least 40% of its dry cell weight. Thus, contrary to the Office's assertion, 40% dry cell weight is not relevant to alginate. Claim 5 refers *inter alia* to various polysaccharides including alginates but is not dependent on claim 2, which in any event refers explicitly only to polyhydroxyalkanoates. Thus, contrary to the Examiner's assertion there is no disclosure in Huisman of a bacterial strain which produces alginate to a level of least 40% of its dry cell weight.

Claim 7 of the Huisman reference which is dependent upon claim 1 contains a list of various bacterial species into which a nuclease gene may be integrated. This includes *Pseudomonas fluorescens* and is the only mention of *Pseudomonas fluorescens* in the entire Huisman document. There is no disclosure which can be derived from the combination of claims 1 and 7 that *Pseudomonas fluorescens* may produce alginate - claim 1 does not refer to alginate and neither does claim 7. There is no disclosure in any part of Huisman that *Pseudomonas fluorescens* may be used to produce alginate at all, let alone at the specified levels of the present claims. The Office's anticipation rejection is improper because the Huisman reference fails to disclose each and every element as arranged of the pending claims. If the Office maintains the present rejection under 35 U.S.C. § 102 Applicants respectfully request that the Office with particularity note where the Huisman reference discloses the elements as arranged in the pending claims.

Therefore, because the Huisman reference fails to disclose each and every element as arranged in the pending claims the Huisman reference fails to anticipate the pending claims.

Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102 be withdrawn.

Conclusion

For the foregoing reasons, Applicants respectfully request that the claims be allowed at this time. A notice of allowance is earnestly solicited.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully Submitted,

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